

Appl. No. 10/561,449  
Amendment dated: January 7, 2009  
Reply to OA of: October 7, 2008

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

Claims 1-44(canceled).

45(currently amended). An In vitro method of generating insulin producing beta cells from a population comprising dedifferentiated exocrine pancreatic cells of a first mammal, said method comprising the steps of:

a) providing a population comprising dedifferentiated exocrine pancreatic cells in a culture medium,

b) adding one or more ligands of the gp130 receptor of a second mammal and/or adding one or more ligands of the EGF receptor of a third mammal to said culture medium,

c) incubating said dedifferentiated exocrine pancreatic cells in said culture medium comprising said one or more ligands of the gp130 receptor and/or said one or more ligands of the EGF receptor,

wherein one of said one or more ligands of the EGF receptor is EGF.

46(previously presented). The method according to claim 45, wherein said ligand of said gp130 receptor is LIF.

47(canceled).

48(previously presented). The method according to claim 45, wherein the method further comprises the step of adding bFGF to said culture medium during step b).

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49(previously presented). The method according to claim 45, wherein said medium is free from KGF or a gastrin/CCK receptor ligand.

50(previously presented). The method according to claim 45, wherein the population comprising dedifferentiated exocrine pancreatic cells is selected from the group consisting of duct cells, acinar cells and islet cells.

51(currently amended). The method according to claim 45, further comprising, prior to step a), a preliminary step of depleting ~~said population from~~ beta cells from said population.

52(currently amended). A population of mammalian pancreatic cells comprising mammalian insulin producing beta cells obtainable by an in vitro method of generating insulin producing beta cells from a population comprising dedifferentiated exocrine pancreatic cells of a first mammal, said method comprising the steps of:

- a) providing a population comprising dedifferentiated exocrine pancreatic cells in a culture medium,
- b) adding one or more ligands of the gp130 receptor of a second mammal and/or adding one or more ligands of the EGF receptor of a third mammal to said culture medium,
- c) incubating said dedifferentiated exocrine pancreatic cells in said culture medium comprising said one or more ligands of the gp130 receptor and/or said one or more ligands of the EGF receptor, wherein one of said one or more ligands of the EGF receptor is EGF.

53(previously presented). The population of mammalian pancreatic cells according to claim 52, wherein said population comprises from about 5 to about 15 percent of insulin- positive cells.

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54(previously presented). The population of mammalian pancreatic cells according to claim 52, wherein said cell population after exposure to 20 mM glucose for 4 hours at 37°C in RPMI-1640 medium supplemented with 10% fetal bovine serum shows a more than 2 fold increase in insulin secretion when compared to the insulin secretion prior to said exposure to glucose.

55(canceled).

56(previously presented). A pharmaceutical composition comprising a therapeutically active amount of a mammalian pancreatic cell population according to claim 52, and at least one pharmaceutically acceptable carrier.

57(withdrawn). A method of prevention or treatment of diabetes type 1 or type 2 comprising administration of a therapeutically effective amount of a combination of a human or humanised ligand of a EGF receptor, and a human or humanised ligand of the gp130 receptor.

58(withdrawn). A method of prevention or treatment of diabetes type 1 or type 2 comprising administration of a therapeutically effective amount of a human or humanised ligand of the gp130 receptor.

59(withdrawn). The method of prevention or treatment according to claim 58, further comprising administration of a human or humanised ligand of a EGF receptor.

60(withdrawn). The method of prevention or treatment according to claim 58, wherein said human or humanised ligand of the gp130 receptor is LIF.

61(currently amended). ~~A population of mammalian pancreatic cells according to claim 52 being identifiable by an~~ An In vitro method for determining the degree of

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redifferentiation of [[a]] the population of mammalian pancreatic cells according to claim  
52: dedifferentiated mammalian pancreatic cells comprising the steps of determining  
one or more parameters selected from the group consisting of:

- a) the presence of CK 20, CK 7 or CK 19,
- b) the occurrence of binucleated cells,
- c) the presence of insulin positive cells,
- d) the presence of C-peptide, Pdx-i and Glut-2,
- e) the presence of gastrin CCKB receptor, PGP9.5 and notch-1 receptor,  
on said mammalian pancreatic cells.

62(new). The method according to claim 1, wherein said cells are grown on a  
surface which is not an ECM surface.